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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/204,865	12/03/98	CHEN	J 9584-006-999

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EXAMINER

LU, F

ART UNIT

PAPER NUMBER

1655

DATE MAILED:

12/16/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.

09/204,865

Applicant(s)

Chen et al.,

Examiner

Frank Lu

Group Art Unit

1655

☒ Responsive to communication(s) filed on Dec 3, 1998

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-56 is/are pending in the application.

Of the above, claim(s) 37-39, 42, 43, and 45-49 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1, 3-5, 7, 8, 12, 14-18, 20-36, 40, 41, 44, and 50-56 is/are rejected.

☒ Claim(s) 2, 6, 9-11, 13, and 19 is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☒ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been
☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 1 and 2

☐ Interview Summary, PTO-413

☒ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

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DETAILED ACTION

Restriction/Election

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

The inventions contain claims directed to more than one distinct species regarding a flow-through device for nucleic acid hybridization.

The species are as follows:

- (1) nucleic acid capture only (claims 1-36, 40,41,44, and 50-56)
- (2) nucleic acid of sequencing ladder only (claims 42, 43, and 45-49)
- (2) nucleic acid recovery required (claims 37-39)

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The species listed above lack the same or corresponding process of making and using. They have distinct physical and chemical properties and different functions and applications.

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Applicants are advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

During a telephone conversation with Ms. Jennifer Weltlich who represents Mr. Samuel Abrams at PENNIE & EDMONDS LLP on December 7, 1999, a provisional election was made without traverse to prosecute the invention of Species 1, claims 1-36, 40, 41, 44, and 50-56. Affirmation of this election must be made by applicant in responding to this office action. Claims 37-39, 42, 43, and 45-49 are withdrawn from further consideration by the examiner, 37 CFR 1.142 (b), as being drawn to a non-elected invention.

Specification

1. The disclosure is objected to because of the following informality: genomic on line 2 of page 30 is misspelled.

Appropriate correction is required.

Claim Objections

2. Claim 22, 54, and 56 are objected to because of the following informality: there should be a coma between "a spin column" and "a microchannel" .

Appropriate correction is required.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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4. Claims 23-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23-36 are rejected as vague and indefinite over word "(i)" of claim 23 because it is unclear how many steps include in this instant claim. For example, does "(i)" mean the first step of multiple steps in this claim? The rejection could be overcome by clarifying this claim.

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claims 1, 3, 12, 15, 23, 26, 27, 32, 36, 40, 41, 44, 53, and 54 are rejected under 35 U.S.C 102 (e) as being anticipated by Feindt *et al.*, (European Patent 0605,828A1, 1994). Feindt *et al.* teach flow-through hybridization assay for oligonucleotides. In this method, different amount of capture DNA were spotted onto Biotodyne B membrane (0.2 or 0.45 or 1.2 μ m from Pall Biosupport Corporation) and wet with NaOH. This flow-through assay device includes Pall Biotodyne B membrane, polycarbonate layer, polyester layer and absorbant layer as shown in Figure 1. The capture DNAs were crosslinked onto the membrane with UV (page 6, line 9-14 and table). The biotinylated target DNA was flowed through the device and finally detected by anti-

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biotin conjugated liposomes containing sulforhodamine B dye (page 6, the fourth paragraph).

Note that flow-through membrane hybridization assay requires no period of incubation of the sample with the membrane (page 3, the fourth paragraph). Thus this prior art meets the limitation of the claims.

Claims 1, 3, 5, 7, 8, 12, 14, 15, 21-23, 27, 29, 31, 32, 40, 41, 44, 53, and 54 are rejected under 35 U.S.C 102 (e) as being anticipated by Tam *et al.*, (US Patent 5741,647, filed on Feb. 16, 1996). Tam *et al.*, teach the determination of a target nucleic acid present in a sample using flow through hybridization device. This device is a multiple-well plate which consists of two stainless plates, two gaskets, one blotting membrane and one temperature regulated controlled block as shown in Figure 1. In this method, the a large number of capture oligonucleotide (20-24 nt), used to capture the target DNA molecules, are covalently immobilized onto the Biotodyne C membrane (page 2, line 1-4). Note that the porous substrate used is Biotodyne C membrane with porosity about 0.45 micron (page 2, the second paragraph, line 4) and $\text{HN}_2\text{-(CH}_2\text{)}_3\text{-moiety}$ on 5' end of a capture oligonucleotides reacts with -COOH group on 3' end of Biotodyne C membrane and forms a covalently carboxyamide linkage (page 12, example IV, line 6-10). Target DNA was amplified by PCR using biotin-11-dUTP and dNTP and was flowed through the device. The hybridization conditions may vary dependent on the experimental conditions. After final washing, the signal could be developed by the incubation with streptavidin-HRP conjugate (page 10, example 1). Thus this prior art meets the limitation of the claims.

Claim Rejections - 35 USC § 103

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6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103 (c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-5, 8, 12, 14-18, 20-25, 27-29, 32, 36, 40, 41, 44 and 50-56 are rejected under 35 U.S.C. 103(a) as being unpatentable over Van Ness *et al.*, (European Patent 0455,905A2, 1991) in view of Fahy *et al.*, (Nucl. Acid Res, 21, 1819-1826, 1993) and further in view of Bio-Rad catalog (page 71,1998/99). Van Ness *et al.* teach the solid supports for nucleic acid hybridization assay. The capture oligonucleotides first were modified at either the 5' or 3' end with a space arm containing a blocked amine group (page 5, the third and fourth paragraphs). After activation, they were covalently linked onto nylon beads treated with alkylating agents. The bead could be employed free in solution, in a flow-through format such as in a column or a dipstick (Page 2, the tenth paragraph). Target oligonucleotide was biotinylated and could be detected by peroxidase-HRP substrate system after the hybridization (page 12, 4 and 5

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paragraphs). Van Ness *et al.* do not teach how to calculate the quantities of capture oligonucleotide in the flow-through device. Fahy *et al.* teach that bromoacetyl and thiol oligonucleotide derivative covalently link onto sulfhydryl- and bromoacetyl-polyacrylamide support (Biogel and Trisacryl resins). The end-attachment efficiencies for the oligonucleotides is greater than 95%. Note that Bio-Gel beads used in this publication are spherical in shape with a diameter ranging from 45 to 180 μm (Bi-Rad Catalog, 1998/99). Thus we can reasonably approximate pores between beads in a column format to be the size of a bead equal to the diameter of the bead even though no exact porous size is available. Fahy *et al.* do not teach to hybridization using a flow-through device. Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to test different hybridization conditions as needed (high, moderate and low stringencies as in claims 24, 25, and 36) and calculate how many captured polynucleotides to attach on a porous substrate (ie. instant claim 4) to decrease and/or increase oligonucleotide end-attachment efficiency using the polyacrylamide supports suggested by Fahy *et al.* as needed for various sample amounts. The paper published by Fahy *et al.* motivates a column format of oligonucleotides as suggested by Van Ness *et al.* and finding proper conditions to perform the flow-through hybridization assay (page 1826, the column 1, the second paragraph).

Allowable Subject Matter

7. Claims 2, 6, 9-11, 13 and 19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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8. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR & 1.821 (a) (1) and (a) (2).

However, this application does not contain, as a separate part of the disclosure on paper copy, a "sequence listing" as required by 37 C.F.R.1.821(c). Furthermore, this application fails to comply with the requirements of 37 CFR & 1.821 through 1.825 because no submission of computer readable form sequences etc. have been submitted. Applicants are given the same response time regarding these matters to comply as that set forth to respond to this office action.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The CM Fax Center number is either (703) 308-4242 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu., Ph.D., whose telephone number is (703) 305-1270. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, W. Gary Jones, can be reached on (703) 308-1152.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

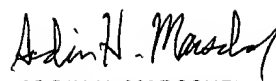
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Frank Lu

December 14, 1999


ARDIN H. MARSCHEL
PRIMARY EXAMINER